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Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in Turkey

Performance of thorax CT in COVID-19 patients

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Abstract
Aim: Chest CT plays an important role in the treatment and diagnosis of COVID-19. It is important to remember that patients with RT-PCR test positive for COVID-19 infection may have normal chest CT.
Material and Methods: This study included patients who underwent RT-PCR and chest CT tests, as well as patients with suspected and confirmed COVID-19 positive cases according to the algorithm of the Institute of Science of Ministry of Health in Turkey were included in this study. The patients were divided into two groups as positive and negative according to RT-PCR results. These groups were divided into two subgroups: with CT findings compatible with COVID-19 and without them. When the RT-PCR test was taken as the gold standard, the specificity, sensitivity, PPV, NPV, and accuracy rates of chest CT were investigated in detecting COVID-19 infection.
Results: RT-PCR was positive in 192 patients and negative in 418 patients. The chest CT scan was positive in 43% (82/192) of 192 patients whose RT-PCR results were positive. Chest CT scan was positive in 25% (108/418) of 418 patients whose RT-PCR results were negative. In 31% of the patients (190/610), chest CT findings were positive for COVID-19. When RT-PCR results were taken as a reference, accuracy, specificity, and sensitivity values in terms of COVID-19 infection of chest CT were 44% (95% CI, 392/610 patients), 43% (95% CI, 82/192 patients), and 74% (95% CI, 310/418 patients) respectively.
Discussion: According to these data, we think that chest CT is not very successful in detecting patients infected with COVID-19, contrary to the literature. Clinicians should always be careful to identify patients with COVID-19 infection with normal thorax CT or negative RT-PCR testing.

Keywords
2019-nCoV; RT-PCR; Computed tomography; Sensitivity; Specificity

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Introduction

In December 2019, a series of "unknown viral pneumonia" cases were reported in Wuhan City, China [1]. The responsible pathogen has been described as the 2019 new coronavirus (2019-nCOV), and the World Health Organization (WHO) has named the associated pulmonary syndrome as Corona Virus Disease-2019 (COVID-19) [2]. Typical clinical signs are fever and cough, in addition to non-specific symptoms such as fatigue, shortness of breath, muscle pain, and headache [3].

It is important to detect infected patients early and keep them away from healthy individuals, because there are no specific vaccines and treatments for COVID-19. Social distancing is the most important strategy to save lives.

A reverse transcription-polymerase chain reaction (RT-PCR) test is required for the diagnosis of COVID-19. However, it takes a long time to obtain test results and produces a certain amount of false-negative results [4]. In a previous study, it was reported that the total positivity rate of RT-PCR for throat swab samples was between 30% and 60% in the first presentation [5]. In this case, RT-PCR with low sensitivity cannot quickly diagnose many of the COVID-19 patients, so these patients will not receive treatment in time. As a result, such patients will cause a rapid spread of the pandemic to a larger population, as the virus is highly contagious. Chest CT is relatively easy to use as a routine imaging tool for diagnosing pneumonia, and it is possible to diagnose pneumonia rapidly using CT. In some studies, it was noted that the RT-PCR test had limited sensitivity, but chest CT might show pulmonary abnormalities compatible with COVID-19 in patients whose RT-PCR results were negative [4, 6]. In the light of this information, it may be thought that chest CT will be useful for the diagnosis of COVID-19. In this study, we compared RT-PCR and chest CT test results in 610 patients suspected of COVID-19 to determine the value of chest CT compared to RT-PCR testing for diagnosis.

Material and Methods

Patient selection

Our study was a retrospective analysis, which was approved by the hospital ethics committee. Patients who applied to Erzurum Regional Training and Research Hospital of Saglik Bilimleri University for COVID-19 between 13 March 2020 and 15 May 2020 were evaluated. Written informed consent was obtained from the patients for the anonymized information to be published in this article. This study included patients who underwent both RT-PCR tests and chest CT and patients with probable and definitive COVID-19 positive cases according to the algorithm of the Institute of Science of Ministry of Health in Turkey were included in this study (Figure 1). RT-PCR results were obtained from the electronic medical records of the Ministry of Health's Public Health Management System (PHMS). If a patient had more than one RT-PCR test, when any of the test results were found positive, the patient was considered to have been diagnosed with COVID-19. A repeated test was performed at intervals of 1 day or more in patients whose first *RT-PCR test was negative.*

The whole patient group underwent a CT scan without contrast within 5 days or less. If more than one chest CT scan was performed on one patient, care was taken to ensure the time interval between RT-PCR test and chest CT less than or equal to 5 days for comparison of diagnostic performance. Patients with a time interval of more than 5 days between both tests were excluded from the study. Atypical and typical chest CT findings were recorded according to chest CT characteristics which were previously described for COVID-19 [4, 5]. The patients were divided into two groups as positive and negative RT-PCR results. These groups were divided into two subgroups: with and without CT findings compatible with COVID-19 (Figure 2). When the RT-PCR test was taken as the gold standard, the specificity, sensitivity, accuracy, NPV, and PPV rates of chest CT in detecting COVID-19 infection were investigated.

Imaging protocol and analysis

All images were obtained in a supine position on a single BT (Aquilion 64, Toshiba, Japan) system. The main features of BT were as follows: matrix = 512 × 512, tube voltage = 120 kVp, pitch = 0.99 - 1.22 mm, automatic tube current modulation (30 - 70 mAs), field of view = 350 mm × 350 mm, slice thickness = 5 mm. All CT images were reconstructed to have a slice thickness of 1 mm. Chest CT images were examined by two radiologists who were blinded to RT-PCR results and had sufficient experience in chest CT interpretation. A decision was made as to whether CT findings were positive or negative. Both radiologists had sufficient information about the patients' clinical symptoms (fever, dry cough, shortness of breath), and their epidemiological history. Radiologists described the features of chest CT. In addition, radiologists divided the patients into two groups, compatible or incompatible with the COVID-19 infection, by reviewing the chest CT images.

Statistical Analysis

Statistical analyzes of the study were performed using the SPSS 23 version (SPSS Inc. Chicago, IL). Categorical variables are shown with frequency and percentage, continuous variables with mean and standard deviation. Negative predictive value, positive predictive value, accuracy, sensitivity and specificity results were calculated by probability ratio based on the RT-PCR result used as the reference (gold standard) in all data sets and subgroups. In the analysis, the confidence interval was determined as 95%. The performance of chest tomography in determining COVID-19 in different age groups and gender variables was also compared with the chi-square test. In the analysis, the degree of significance was taken as 0.05.

Results

General description:

Ten patients with a time interval of more than 5 between RT-PCR testing and chest CT were excluded from the study. The mean time interval between RT-PCR test and chest CT was determined as 1 day (time interval 0-5 days). The working flow diagram is shown in Figure 2. RT-PCR was positive in 192 patients and negative in 418 patients. In 31% of the patients (190/610), chest CT findings were positive for COVID-19. The main findings of chest CT scans of patients were ground-glass opacities (97% [185/190]) and consolidations (87% [166/190]) (Table 1). Chest CT scan was positive in 41% (80/192) of 192 patients whose RT-PCR results were positive. Chest CT scan was positive in 25% (108/418) of 418 patients whose RT-PCR results were negative.

Table 1. Characteristics of 610 patients

Specifications	Results
Gender	
Female	252 (41)
Male	358 (59)
Age (year)	
Average Age	48 ± 20 (Between 18 and 96)
< 20	15 (2)
20-39	224 (37)
40-59	177 (29)
≥ 60	194 (32)
RT-PCR test results	
Positive	192 (31)
Negative	418
Thorax CT findings	
Compatible with COVID 19	**190 (31)**
single lobe	48/190 (25)
multiple lobes	139/190 (73)
one-two lesions	49/190 (26)
many lesions	132/190 (69)
ground glass	185/190 (97)
consolidation	166/190 (87)
nodule	82/190 (43)
fibrosis	25/190 (13)
reverse halo	3/190 (2)
crazy-paving	55/190 (29)
cavite	0/190 (0)
pruned tree	15/190 (8)
vascular dilation	24/190 (13)
interlobular septal thickening	41/190 (22)
bronchodilation	4/190 (2)
pleural thickening	1/190 (1)
pleural fluid	23/190 (12)
LAP	1/190 (1)
Normal	**420 (69)**
Median time interval between chest CT scan and RT-PCR test (days)	**1 (Between 0 and 5)**

Note: Values in parentheses indicate the percentages of the data. The mean and standard deviation was taken at age. The time interval is given as median.

Table 2. Chest CT performance for COVID-19 infection by RT-PCR

	Results (n)				Test Performances (%)				
	TP	TN	FP	FN	Sensitivity [95% CI]	Specificity [95% CI]	PPV [95% CI]	NPV [95% CI]	Accuracy [95% CI]
General	82	310	108	110	43 (82/192) [35-50]	74 (310/418) [70-78]	96 (82/190) [96-97]	6 (310/420) [6-7]	44 (392/610) [40-48]
Age									
<60	60	194	62	100	37 [30-45]	76 [70-81]	97 [96-98]	6 [5-7]	39 [35-44]
≥60	22	116	46	10	69 [50-84]	72 [64-78]	98 [97-98]	11 [7-17]	70 [62-75]
Gender									
Male	42	193	59	64	40 [30-50]	77 [71-82]	97 [96-98]	6 [5-7]	41 [36-47]
Female	40	117	49	46	47 [36-58]	70 [63-77]	97 [96-98]	6 [5-8]	48 [41-54]

TP= true positive, TN=true negative, FP=false positive, FN=false negative, PPV= positive predictive value, NPV=negative predictive value. Values in parentheses are the number of patients used to calculate percentages. Data values in square brackets indicate the confidence interval.

Table 3. Chi-square test results

Chi-square test results										
	Sensitivity		Specificity		PPV		NPV		Accuracy	
	x^2	p	x^2	p	x^2	p	x^2	p	x^2	p
Gender	2.91	0.08	4.13	0.04*	0.00	0.94	0.95	0.32	2.90	0.08
Age	54.29	0.000**	1.00	0.31	0.8	0.36	4.39	0.03*	51.41	0.000**

*p<0.05 **p<0.000

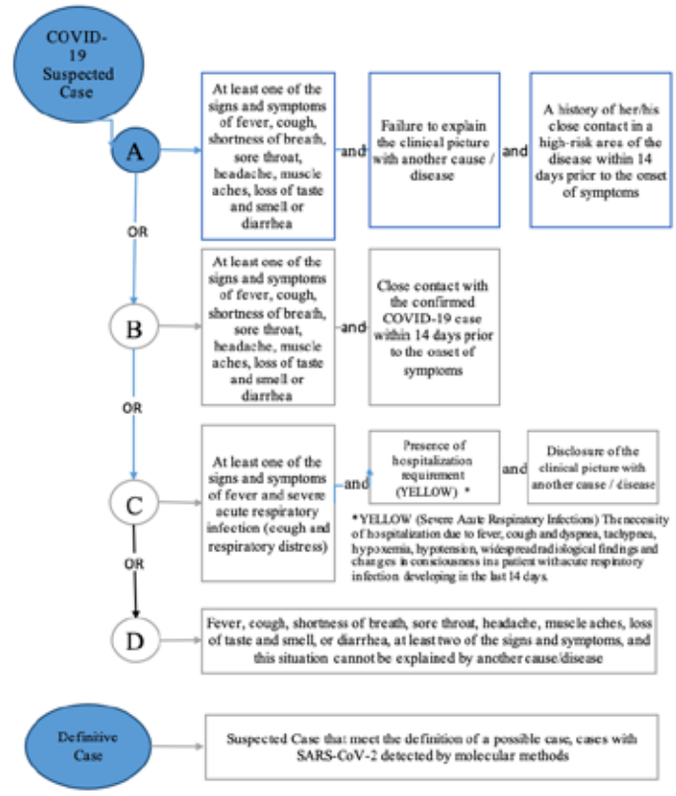

Figure 1. Case algorithm

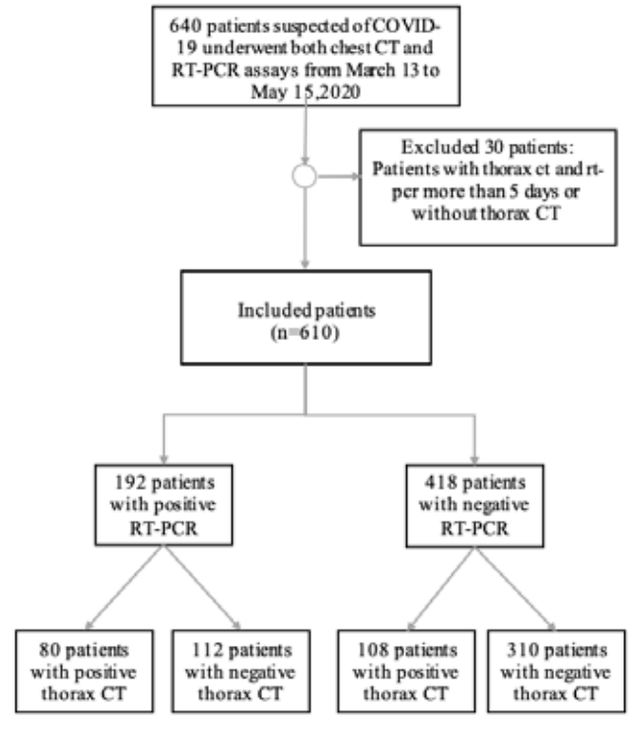

Figure 2. Work flow chart

Performance of Chest CT in the diagnosis of COVID-19:

One hundred ninety patients had positive chest CT findings. When RT-PCR results were taken as a reference, accuracy, sensitivity, and specificity values in terms of COVID-19 infection of chest CT were 44% (95% CI, 392/610 patients), 43% (95% CI, 82/192 patients), and 74% (95% CI, 310/418 patients), respectively. The performance of chest CT in the diagnosis of COVID-19 in age and gender groups is shown in Table 2.

When thorax CT was evaluated in the diagnosis of COVID-19, there was no significant difference between men and women in terms of accuracy, sensitivity, NPV, and PPV (p = 0.08, 0.08, 0.32, 0.94 and, respectively). However, the specificity of thorax CT was higher for men than for women, and this difference was significant (p = 0.04) (Table 3).

The sensitivity, NPV, and accuracy values of chest CT in patients over the age of 60 were higher than patients under the age of 60. This difference was also statistically significant (p = 0.000, 0.03, 0.000, respectively). There was no difference in specificity and PPV between <60 and ≥60 (p = 0.31, 0.36, respectively) (Table 3).

Patients with a negative first RT-PCR test and a positive RT-PCR in subsequent tests:

In our study, the first two RT-PCR test results were negative in three out of 33 patients (two-day test interval), and the third RT-PCR results were positive. Two of these patients had positive chest CT findings compatible with COVID-19. In 30 patients, the first RT-PCR test results were negative, and the second RT-PCR tests performed within two days were positive. Among these 30 patients, 17 had CT findings consistent with COVID-19.

Discussion

An increase in the number of infected patients during a pandemic is inevitable. As a result of this, there will be an unmet level of the RT-PCR kit which is necessary for the diagnosis of COVID-19. According to the algorithms, the RT-PCR test has an important place in the isolation of patients or the decision of hospitalization. Some studies show that RT-PCR has low sensitivity in detecting patients infected with COVID-19. There are a lot of reasons for low sensitivity, such as low viral load, poor nucleic acid detection technology, and inappropriate clinical sampling. In our study, the positivity rate of RT-PCR test for swab samples taken from the nose and throat regions was found to be 31% (95% CI), similar to the previous study by Yang et al (30 - 60%) [5].

Studies show that characteristic CT features of COVID-19 are ground-glass opacity, and multifocal pneumonic infiltrations [6, 7, 8]. In our study, the results of chest CT of the patients with COVID-19 were as follows: multiple lobes 73% (139/190), multiple lesions 69% (132/190), ground-glass opacity 97% (185/190), consolidation 87% (166 / 190), vascular dilatation 13% (24/190), and crazy-paving sign 29% (55/190). These findings were consistent with previous findings in the literature. Chest CT reveals many findings in COVID-19 patients as in our study. The severity and stage of the infection are shown as the reason why these findings are variable and varied [9]. However, these findings are not specific to COVID-19. They can be seen in other viral and atypical infections as well. Therefore, we cannot distinguish COVID-19 from other viral types of pneumonia, such as Severe Acute Respiratory Syndrome and Middle East Respiratory Syndrome, using chest CT [10, 11].

Some studies have shown that chest CT has a higher sensitivity than RT-PCR in detecting patients infected with COVID-19 [12]. According to this, it is thought that chest CT may be a more sensitive, practical, and fast method to diagnose and evaluate COVID-19, especially in the pandemic regions. When we take RT-PCR results as a reference in our 610 disease series, the accuracy, specificity, and sensitivity of chest CT in terms of COVID-19 infection are 44% (95% CI, 392/610 patients), 74% (95% CI, 310/418 patients) and 43% (95% CI, 82/192 patients), respectively. Our study has shown that chest CT is not sensitive enough for COVID-19.

In previous studies, conducted by Zhong et al and Tao et al, positive chest CT ratios were 76.4% and 97% in RT-PCR positive COVID-19 patients, respectively. In addition, Tao et al also demonstrated that more than 70% of patients with negative RT-PCR tests had typical chest CT findings compatible with COVID-19 [13, 14]. In our study, the rate of patients with chest CT findings among patients who were RT-PCR positive (true positive) was 41% (80/192). This may be due to the early diagnosis of these patients. The rate of patients with chest CT findings among patients who had negative RT-PCR results was 25% (108/418).

Unlike other previous studies, our study has shown that the false positive rate of CT is low. Our first goal is to isolate patients and implement appropriate treatment for the COVID-19 outbreak. Even some false positives of CT could be accepted to provide rapid control of the disease. However, our study has shown that CT has low performance in detecting true positives.

According to these data, we think that chest CT is not very successful in detecting patients infected with COVID-19, contrary to the literature. In the literature, there are studies showing that patients with RT-PCR positive COVID-19 infection may have a normal chest CT at admission [12, 14, 15]. When these studies and our study are evaluated together, it is concluded that the normal evaluation of chest CT cannot rule out the diagnosis of COVID-19, especially in patients who are symptomatic in the early period. Although the RT-PCR test has a false negative rate to some extent, the RT-PCR test remains the gold standard to make a definitive diagnosis of COVID-19. The conclusion we draw from our series is that chest CT may be a diagnostic aid rather than a diagnostic tool.

Conclusion

It is important to diagnose patients with COVID-19 at an early stage and isolate them from the community in terms of ending the pandemic. In addition, early diagnosis of these patients will decrease the mortality rates. However, neither RT-PCR nor chest CT can do this alone. Using the two tools together will make the job of clinicians seriously easier for us.

After all, the virus tests all of us. We need to figure out how good RT-PCR or thorax CT is to pass this test.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
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